

Wake Up





Liver Cirrhosis

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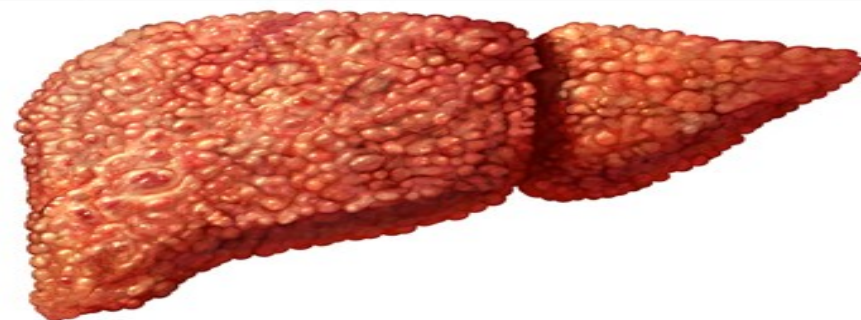
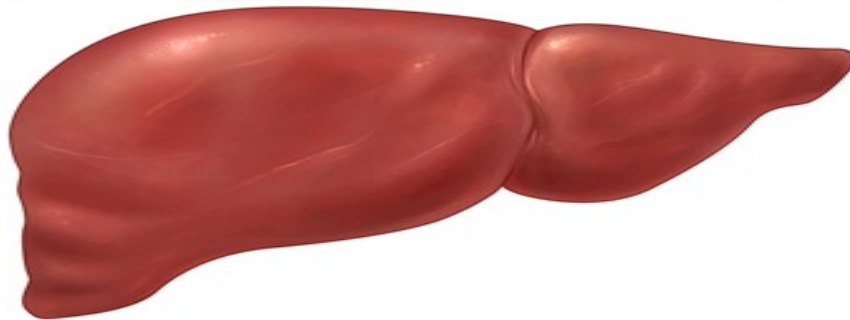
Liver Cirrhosis



Normal Liver



Liver with Cirrhosis



INTENDED LEARNING OBJECTIVES (ILO)



- Classify cirrhosis
- Explain pathogenesis and complications of cirrhosis and portal hypertension
- Determine symptoms & signs of liver cirrhosis
- Correlate pathologic features of cirrhosis with the clinical picture ,investigations and complications
- Approach diagnosis of liver cirrhosis
- Plan for management of liver cirrhosis



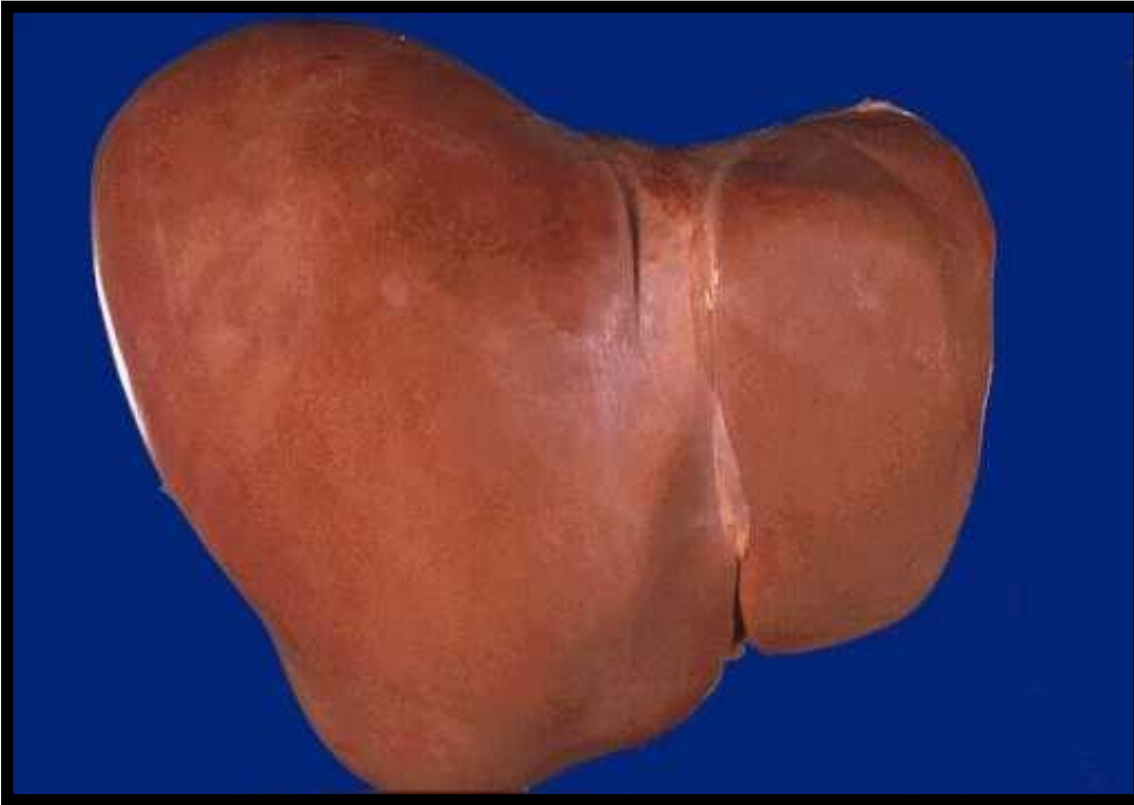
Definition

- Chronic progressive diffuse liver disease
- Characterized by conversion of normal hepatic architecture into structurally abnormal nodules by fibrosis
- End result of chronic liver disorders

Liver Cirrhosis

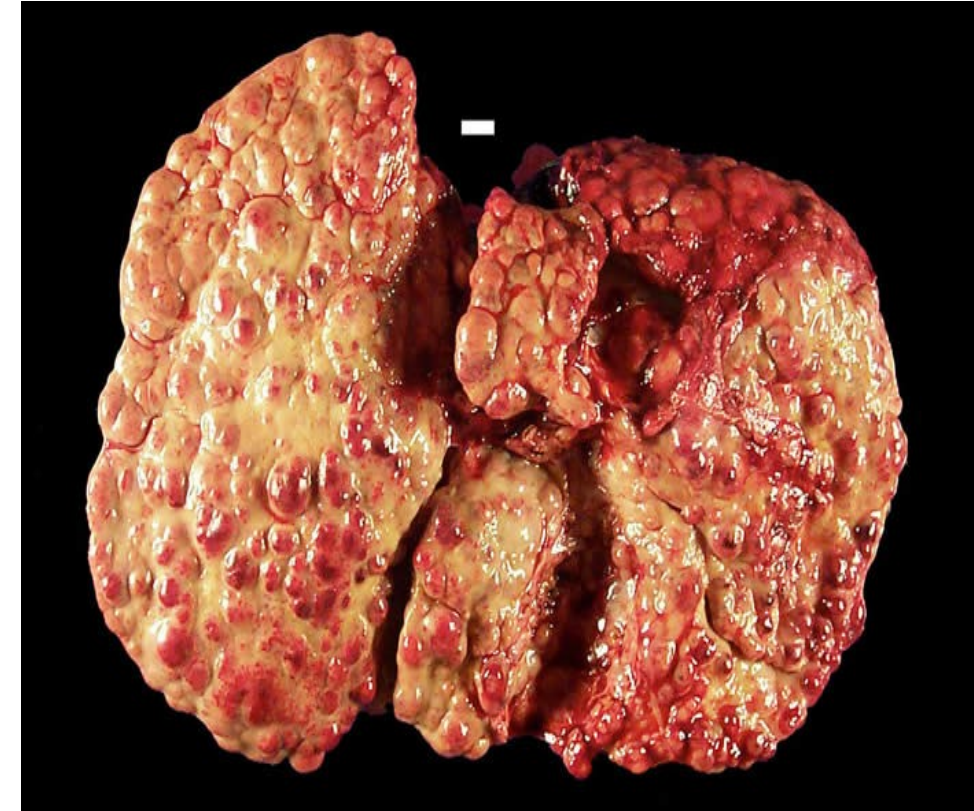


Normal Liver



<https://webpath.med.utah.edu/jpeg4/LIVER002.jpg>

Cirrhosis

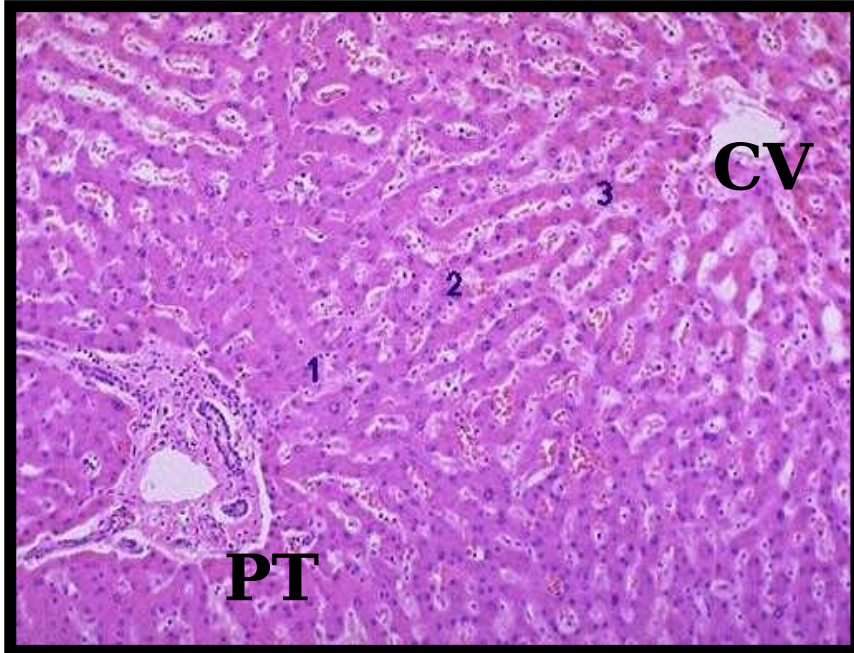


<https://3.imimg.com/data3/TP/XL/MY-2297891/hydatid-cysts-of-the-liver-125x125.jpg>

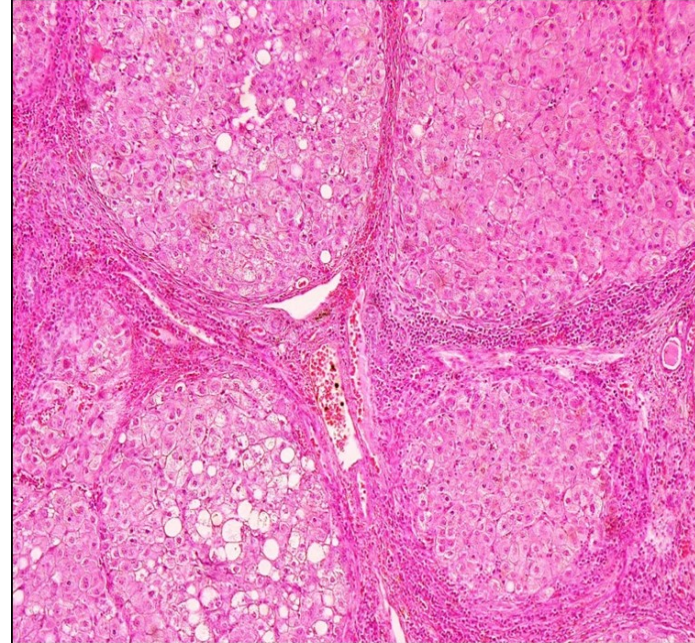
Liver Cirrhosis



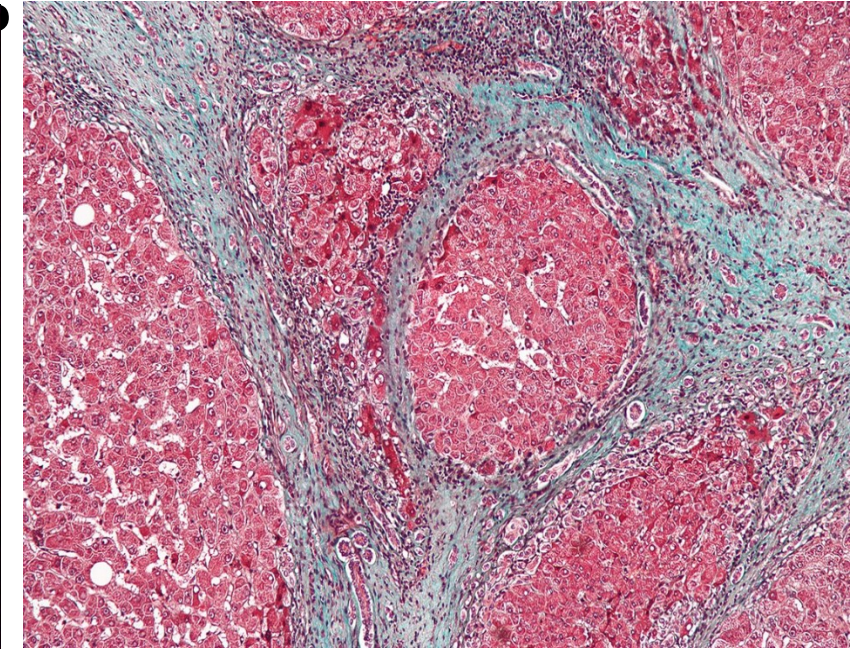
=Fibrous septa + Parenchymal nodules of regenerating hepatocytes
Cirrhosis



**Collagen in liver capsule
portal tracts around
central veins.**



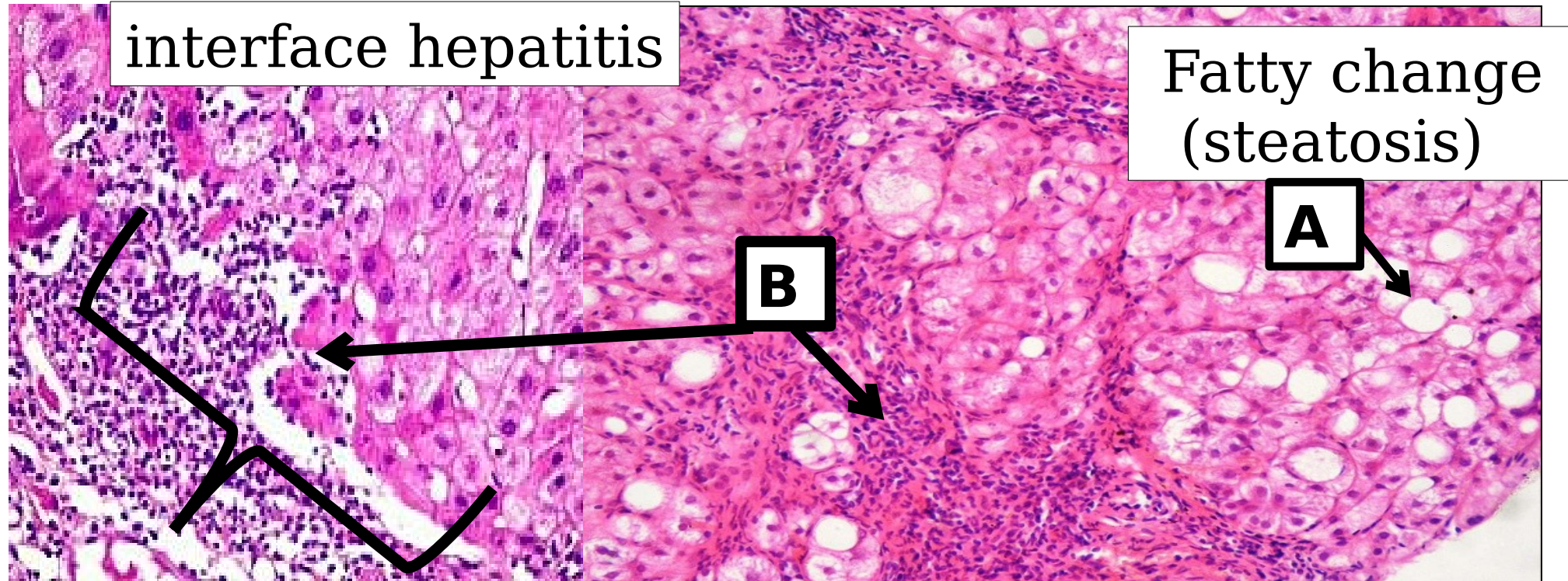
**Nodules
separated by
fibrous tissue
septa**



**Masson
Trichrome stain**

<https://i.pinimg.com/originals/06/52/3a/06523a40c7ae308cb8956cb46a3cada9>

• “Active” Liver cirrhosis



**Fibrous tissue >>inflammation + interface &
or lobular hepatitis**

Explain pathogenesis of Cirrhosis

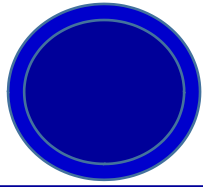


**Hepatocytes
death**

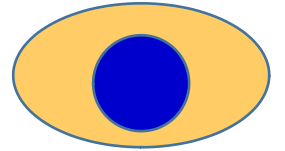
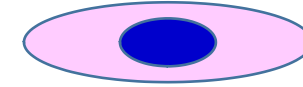
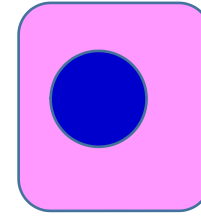
**ECM
deposition**

**vascular
reorganizatio
n.**

Explain pathogenesis of Cirrhosis



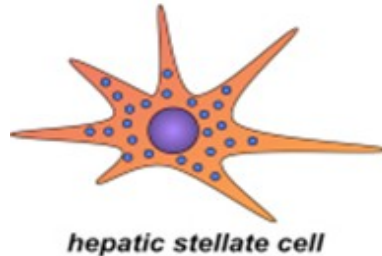
Chronic inflammatory cells



Injured Cells: hepatocytes, endothelial & Kupffer cells

Increase Cytokines & growth factors

Perisinusoidal Stellate Cells (Ito cells)



hepatic stellate cell



Myofibroblast

Collagen deposition & ECM

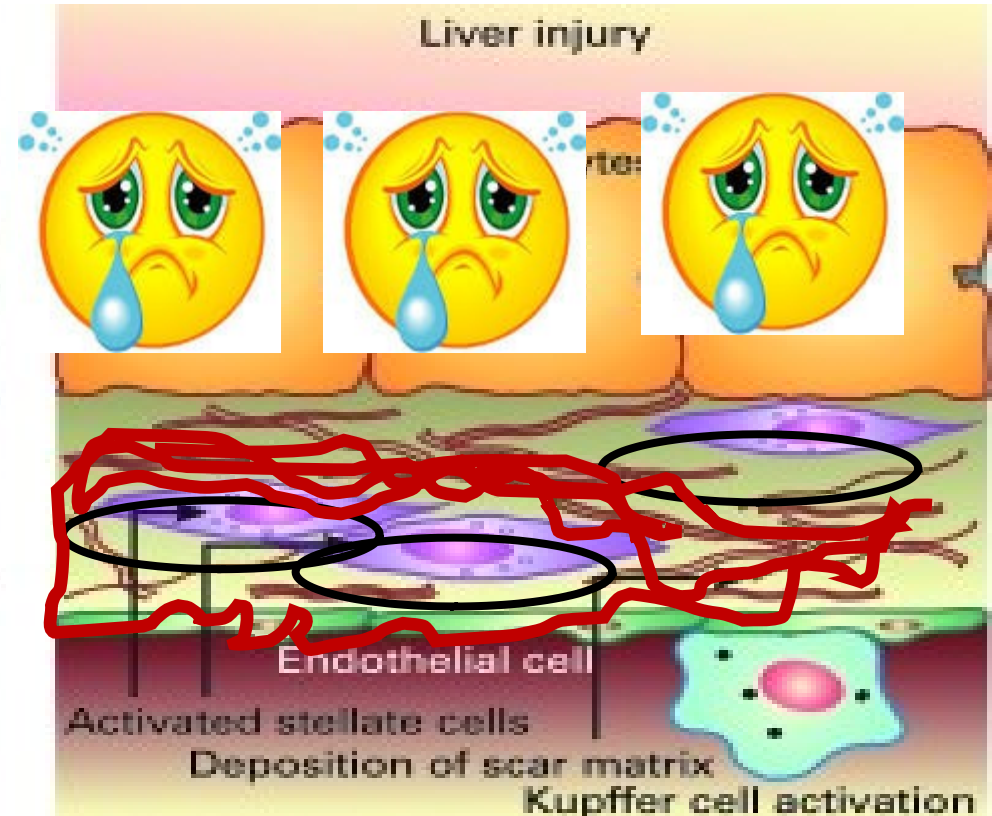
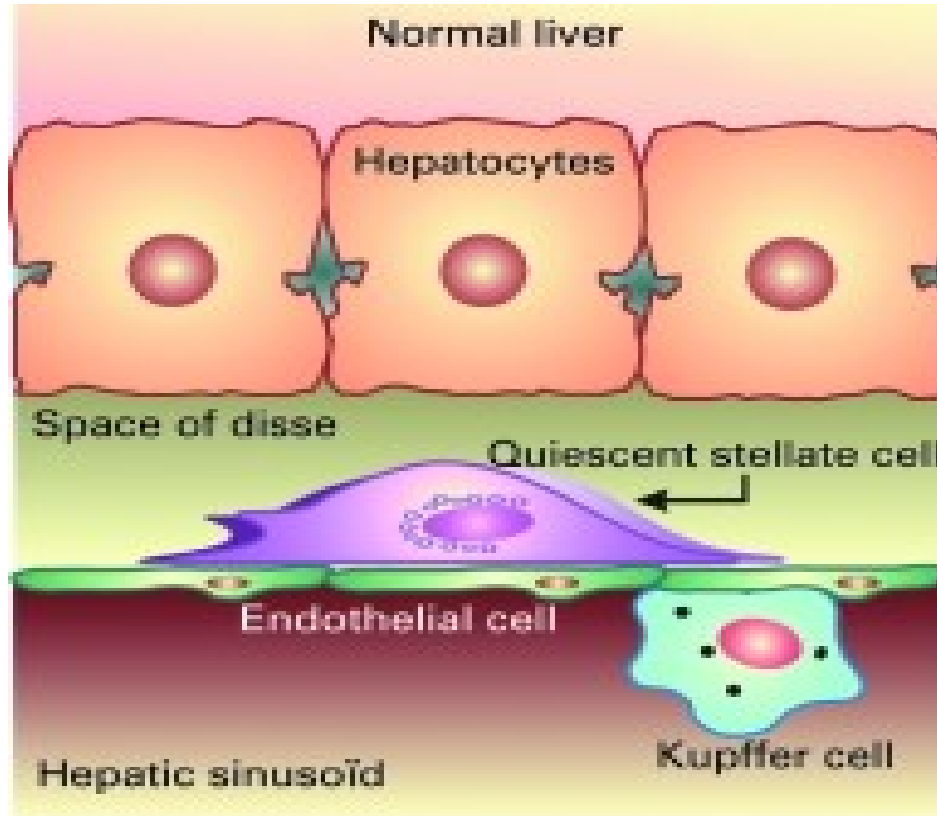
nodule formation

Pathogenesis of Cirrhosis



1-Hepatocyte death

2 -ECM deposition

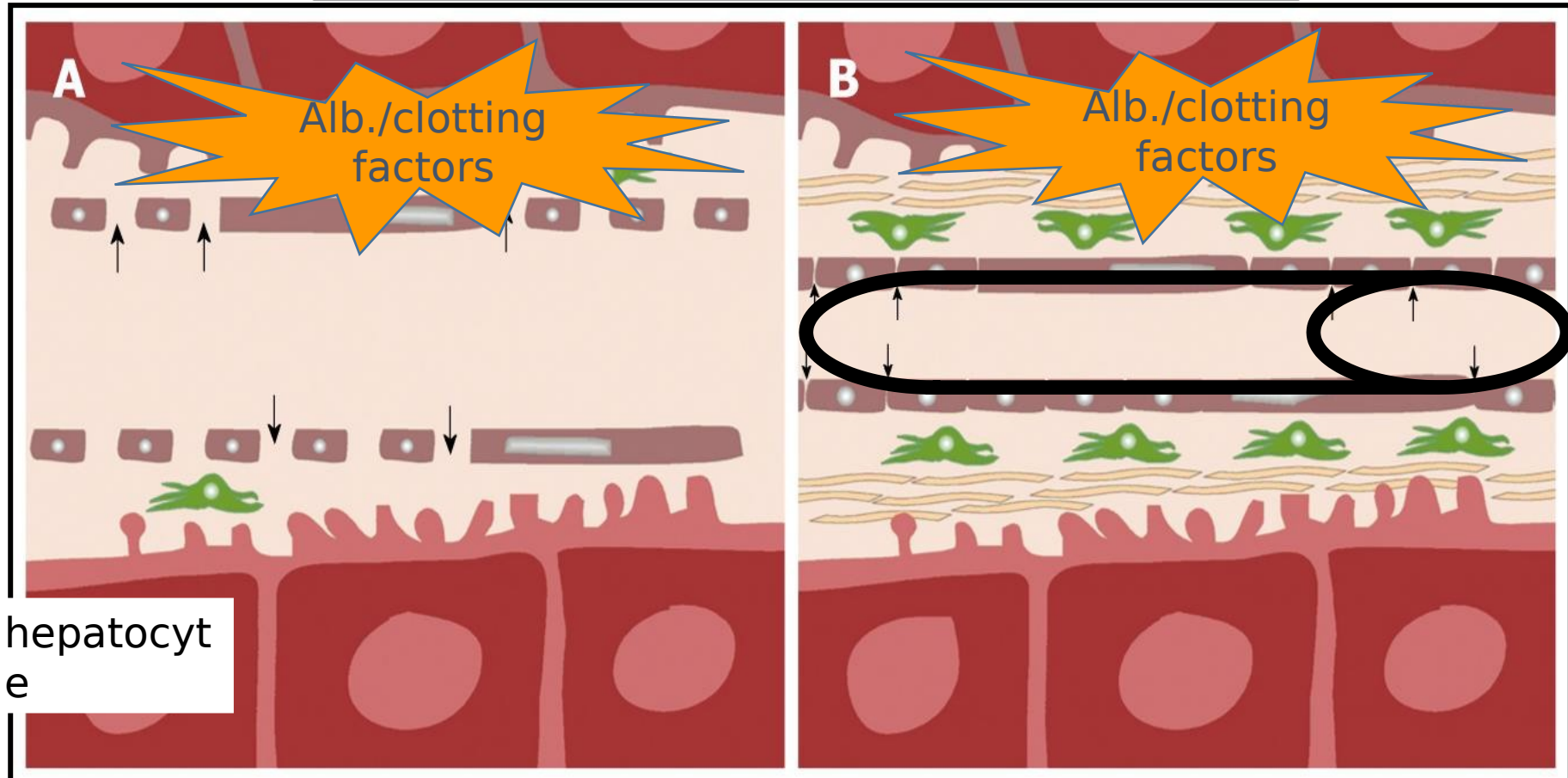


Liver injury >>activation of stellate cells >>transform into myofibroblasts >>produce collagen leading progressive fibrosis
closure of endothelial fenestrations

Pathogenesis of Cirrhosis



3-Vascular reorganization.



<https://f6publishing.blob.core.windows.net/8d07584b-ca71-439b-8de5-a29fbcc57bc7/WJG-16-1598-g002.jpg>

loss of sinusoidal
endothelial cell

Pathogenesis of Cirrhosis (Summary)



1. Hepatocyte death , stimulated kupffer cells , endothelial cells chronic inflammation increase production of cytokines (TNF), (IL-1),

2. Extracellular matrix deposition

- Cytokines stimulate **perisinusoidal stellate cells (Ito cells)** to transform into a **myofibroblast-like cell**
- Activated stellate cells (myofibroblast) stimulate collagen synthesis
- Portal fibroblasts also participate in some forms of cirrhosis.



3. Vascular reorganization

- Collagen deposition leads to loss of sinusoidal endothelial cell fenestrations
- Conversion of sinusoids to higher pressure, fast-vascular channels without solute exchange.
- In particular, the movement of proteins (e.g., albumin, clotting factors, lipoproteins) between hepatocytes and the plasma is markedly impaired.
- High pressure in portal circulation leads to development of porto-systemic vascular shunts

Effects of cirrhosis (Quiz)



What are the effects of cirrhosis you expect?



higher sinusoidal & portal pressure

Impaired exchange of solutes between plasma & hepatocytes

Pathogenesis of cirrhosis (Quiz)



Name the cell responsible for collagen deposition in cirrhosis

Ito cell



Classification of Cirrhosis



I. Morphological Classification

Micronodular, Macronodular, Mixed cirrhosis (size of nodules)

II. Aetiological Classification

1. Viral (B , C or B with D)
2. Autoimmune hepatitis
3. Alcoholic/NAFLD
4. Drugs & Toxins
5. Biliary (Chronic Cholestatic liver disease)
6. Metabolic
 - a. Hemochromatosis
 - b. Wilson's disease
 - c. α 1 antitrypsin deficiency
7. Cryptogenic (unknown) (now known as burned out NASH)

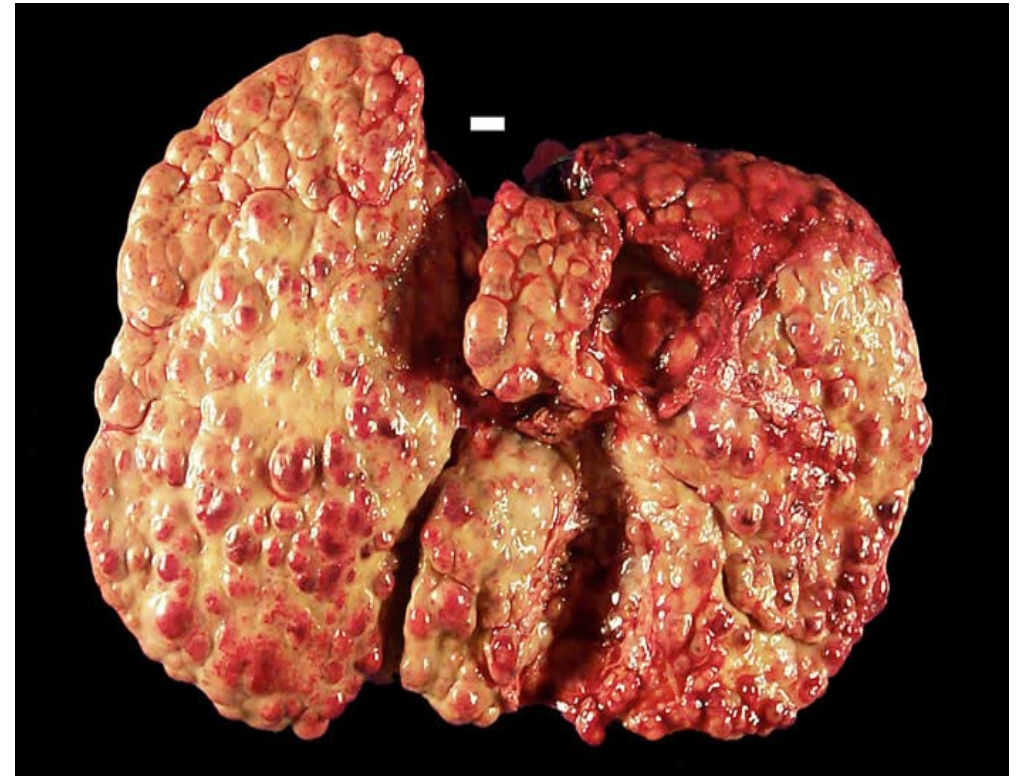
Classification of Cirrhosis



<https://library.med.utah.edu/WebPath/jpeg4/LIVER011.jpg>

Micronodular Cirrhosis

- Each nodule measures **less than 3 mm** in diameter



<https://3.imimg.com/data3/TP/XL/MY-2297891/hydatid-cysts-of-the-liver-125x125.jpg>

Macronodular Cirrhosis

- Each nodule measures **more than 3mm** in diameter

Clinical picture of cirrhosis



Symptoms

- Fatigue
- Yellow discoloration in the skin and eyes (jaundice)
- Leg swelling (edema)
- Abdominal swelling (ascites)
- Bleeding or bruising tendency

Symptoms



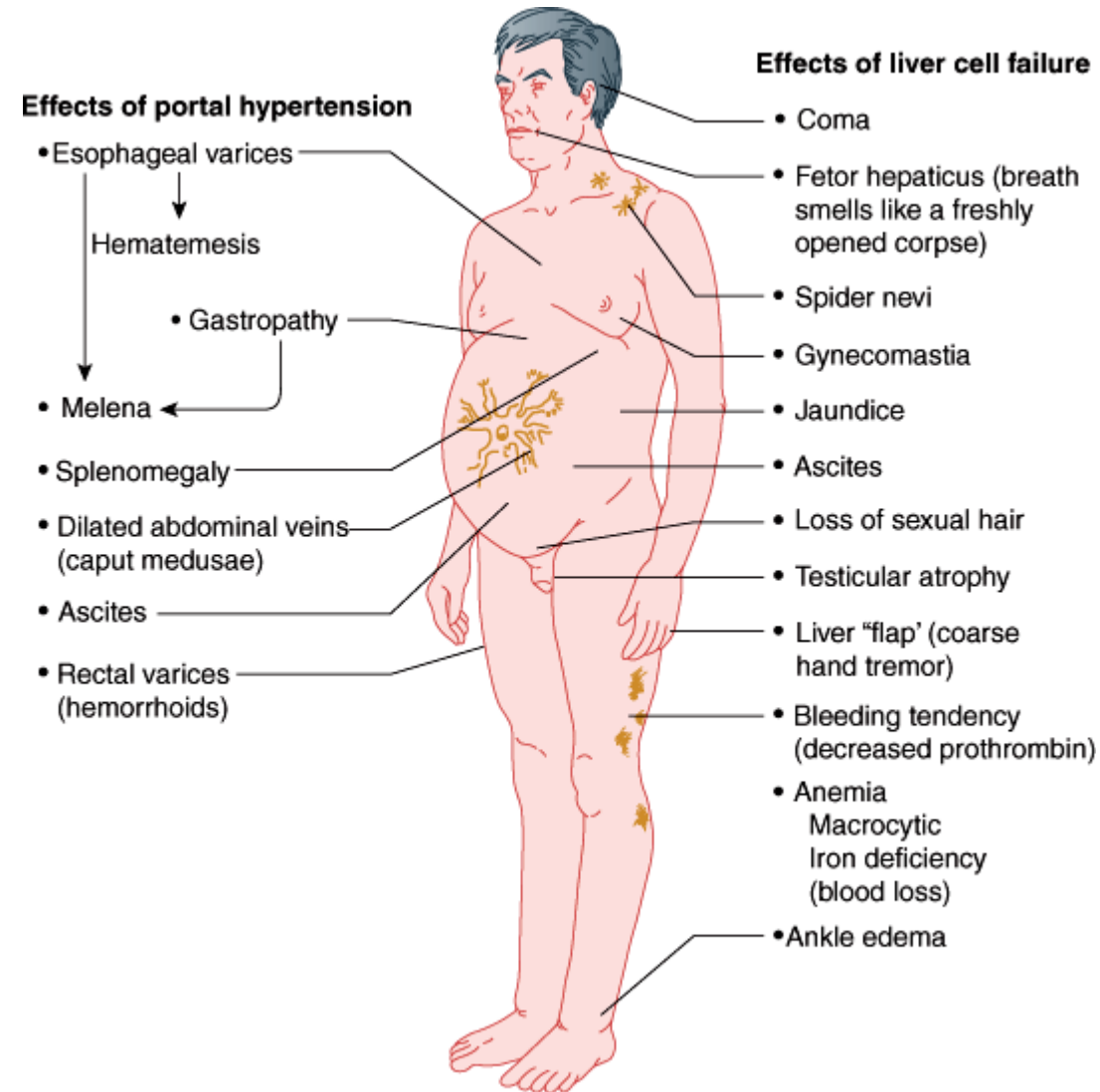
- Itchy skin
- Spiderlike blood vessels on your skin
- Redness in the palms of the hands
- Loss of appetite
- Nausea
- Weight loss

Symptoms



- For women, absence of menstruation
- For men, breast enlargement (gynecomastia) or testicular atrophy with loss of libido
- Disturbed consciousness (hepatic encephalopathy)

Signs of Liver Disease



Signs of Liver Disease



(increased bilirubin due to dysfunction of bilirubin metabolism)



(impaired breakdown of sex hormones)



(hypoalbuminemia)



Signs of Liver Disease



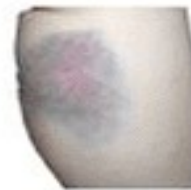
(dilated veins around the umbilicus due to portal htn)



(impaired breakdown of estrogens)



(isolated telangiectasias)



(defective coagulation)



(abnormal motor fct due to hepatic encephalopathy)

**FEETOR
HEPATICUS**

(characteristic odor due to volatile aromatic compounds)

Investigating Liver Disease



Tissue	Imaging and Interventions	Laboratory
Liver Biopsy	Ultrasound	Liver Enzymes (ALT,AST,ALP,GGT)
	CT (Triphasic)	Liver Functions (Albumin, Bilirubin, INR)
	MRI	Viral Markers (HCV-Ab, HBsAg, PCR)
	MRCP	Autoimmune Markers (ANA, ASMA, IgG, AMA, ANCA)
	ERCP	Complete Blood Count
	Endoscopy	Kidney Functions
		Others (A1AT, Copper, ...)

Complications of Cirrhosis



1. Portal hypertension

2. Hypoalbuminemia

3. Impaired clotting factor synthesis

4. Failure of inactivation of estrogen >>?

5. Liver cell failure

6. Hepatocellular carcinoma (HCC)

Complications of Cirrhosis

?What is Portal Hypertension-1



Def: Increase of portal pressure > 5-10 mmHg

Pathogenesis:

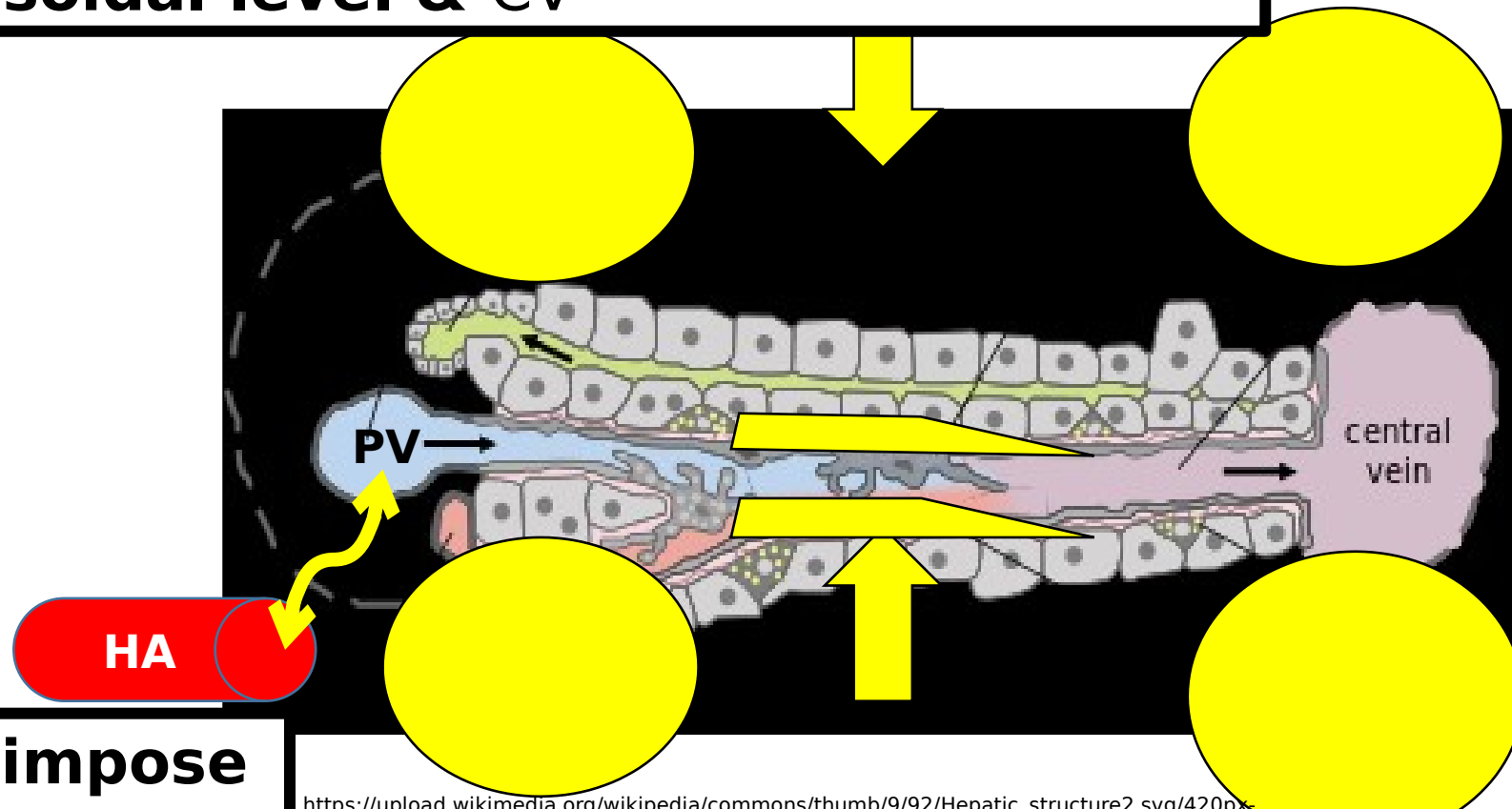
- 1. Increased resistance to flow at sinusoidal level & CV**
- 2. Compression of portal vein radicles & CV by regenerating nodules**
- 3. Anastomosis between **arterial** & **portal** systems in the fibrous bands > > Porto-systemic shunts**

Pathogenesis of Portal Hypertension



(1) Increased resistance to flow at sinusoidal level & CV

<https://www.youtube.com/watch?v=Cox6Z5pqMBo>



3. Shunt impose arterial pressure on portal V

(2) compression of portal vein radicles & CV by regenerating nodules

https://upload.wikimedia.org/wikipedia/commons/thumb/9/92/Hepatic_structure2.svg/420px-Hepatic_structure2.svg.png

Complications of Cirrhosis

Effects of Portal Hypertension-1



a. Ascites



<https://www.homeremedyhacks.com/wp-content/uploads/2017/07/ascites-696x536.jpg>

b. Splenomegaly & hypersplenism >> Pan cyto



<https://image.slidesharecdn.com/6stevekorblau-150518171041-lva1-app6891/95/treatment-of-high-risk-myelofibrosis-20-638.jpg?cb=1431969714>

Complications of Cirrhosis

Effects of Portal Hypertension-1



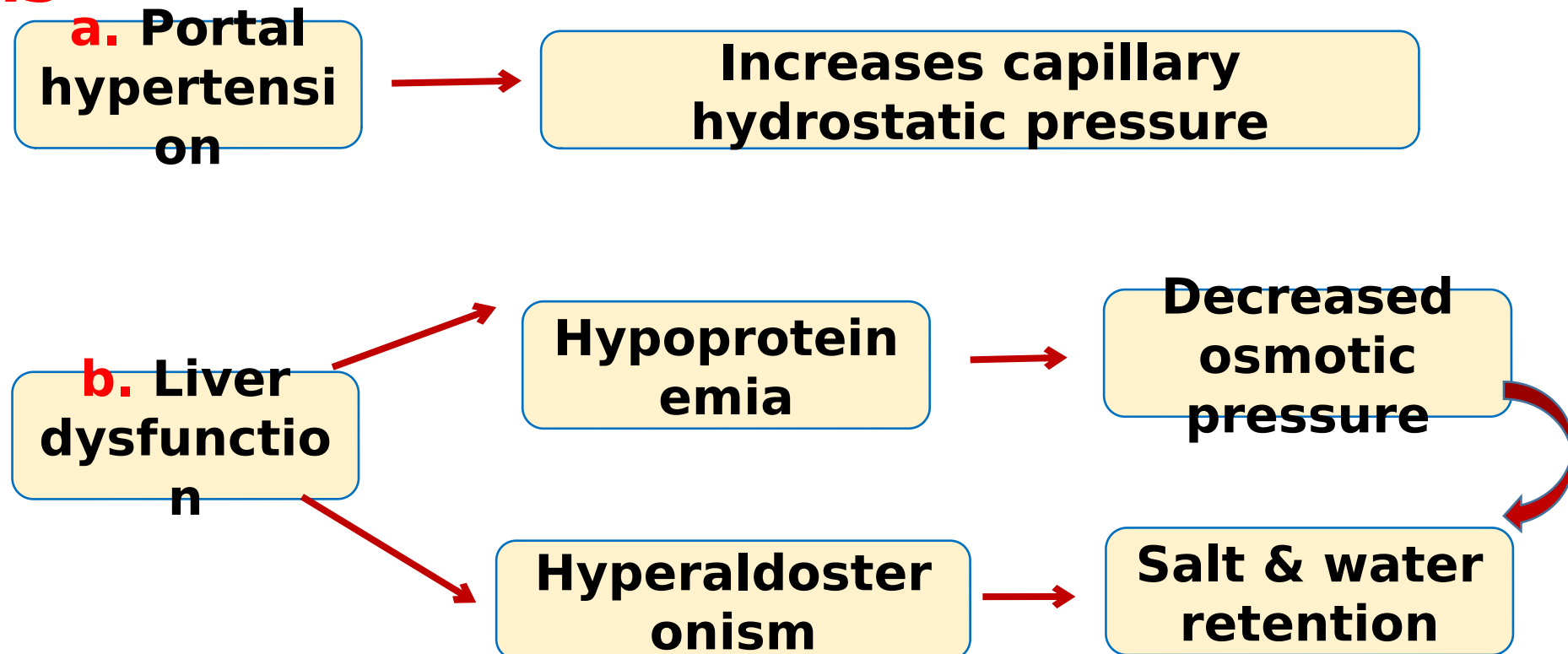
a. Ascites

Def: Collection of excess fluid in the peritoneal cavity.

Pathogenesis



<https://upload.wikimedia.org/wikipedia/commons/a/a3/Hepaticfailure.jpg>

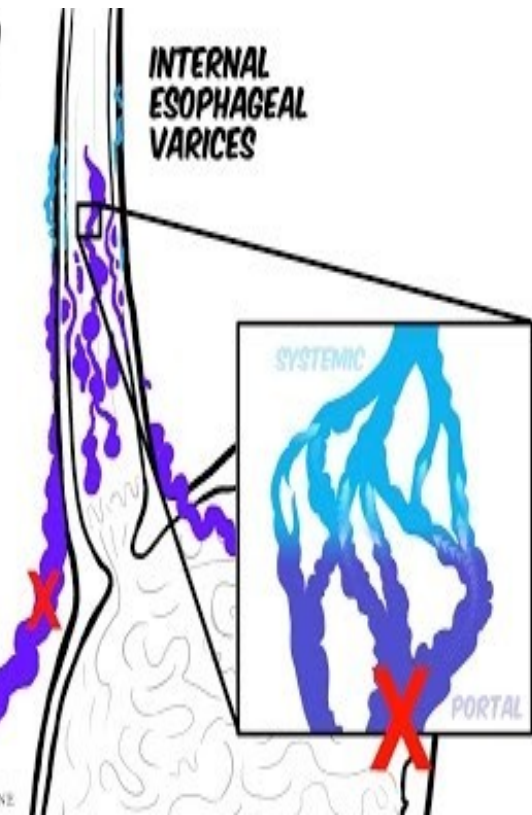


Complications of Cirrhosis

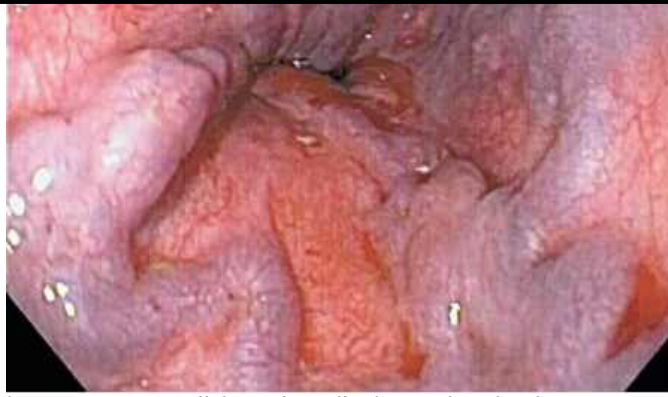
Effects of Portal Hypertension-1



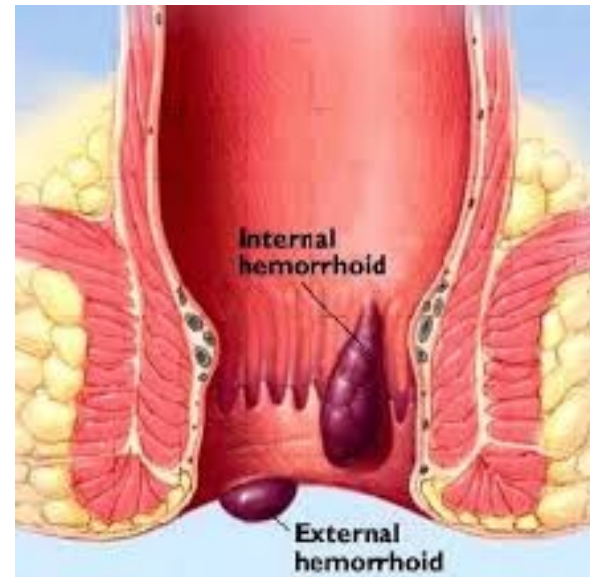
c.Portosystemic shunts



**MOST
DANGEROUS IN
PH
>>> Hematemesis**



https://accessmedicine.mhmedical.com/data/books/2129/bnim20_ch315_f033.png



https://assets.lybrate.com/q_auto:eco,f_auto,w_450/imgs/dt/tp/6ceb59583cbb68a58d64d95bd5156bde/a8924d452ce784322eef791a429583a2/c5e62e.jpg



https://i0.wp.com/images-prod.healthline.com/hlcmsresource/topic_centers/4174-Caput_Medusae_642x361.jpg?w=1155

Esophageal varices

Piles

Caput medusae

<https://i.ytimg.com/vi/Cox6Z5pqMB0/maxresdefault.jpg>

Complications of Cirrhosis



2. Hypoalbuminemia : edema & ascites

**3. Impaired clotting factor synthesis & hypersplenism : bleeding >
(Prothrombin Time prolonged)**

4. Failure of inactivation of oestrogen :
• **Testicular atrophy & gynecomastia in males**

• **Amenorrhea in females**

GIT & Metabolism



<https://integrityskin.com.au/wp-content/uploads/2016/02/Integrity-Paramedical-Skin-Practitioners-Brisbane-Laser-Clinic-Spider->

<http://medicalpoint.org/wp-content/uploads/2016/01/palmar->

A silhouette of a human head in profile, facing right, against a dark blue background. Inside the head, there is a white oval shape containing the text "Ammoni a" in black, bold, sans-serif font. The text is split across two lines: "Ammoni" on the top line and "a" on the bottom line. The head silhouette is dark, and the brain area is visible in a lighter blue shade.

Neuropsychiatric disturbances (apathy, disorientation, tremors & finally coma) with liver dysfunction

Complications of Cirrhosis



6. Hepatocellular Carcinoma



https://www.pharmaceutical-technology.com/wp-content/uploads/sites/10/2018/06/Hepatocellular_carcinoma_1.jpg

Complications of Cirrhosis (summary)

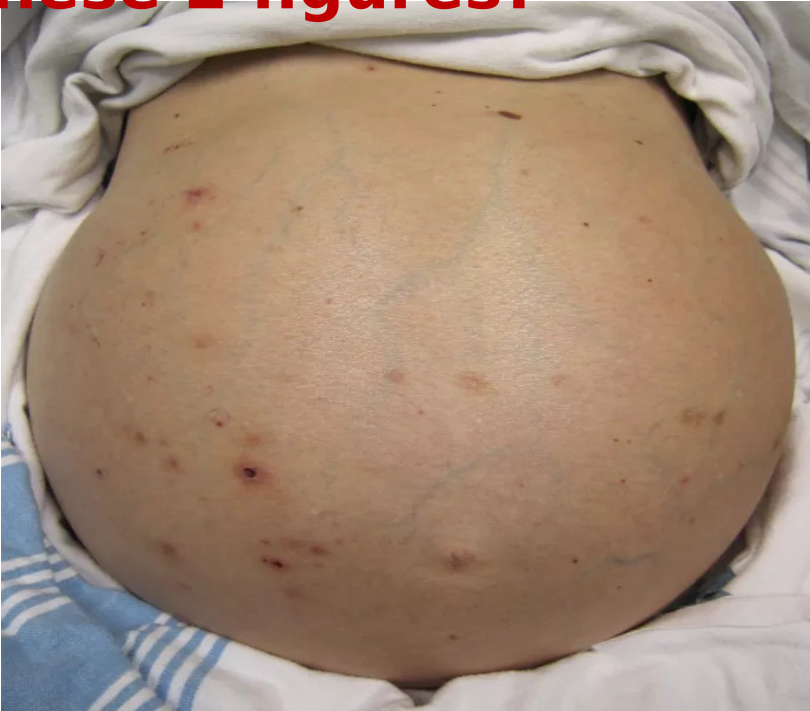


1. Portal hypertension leading to
 - Ascites**
 - b. Splenomegaly > hypersplenism**
 - c. Portosystemic shunts**
 - **Esophageal varices**
 - **Piles**
 - **Caput medusa**
2. Oedema & ascites (hypoproteinaemia & PH)
3. Bleeding tendency (dt hypersplenism &)
4. Failure of inactivation of oestrogen >>
 - testicular atrophy & hyperplasia of breast in males
 - (gynaecomastia) & amenorrhoea in females
 - Spider nevi - Palmar erythema
5. Hepatic failure & encephalopathy
6. Hepatocellular carcinoma

Complications of Cirrhosis (Quiz)



What are the effects/Complications of cirrhosis present in these 2 figures?



Ascites & bleeding

<http://upload.wikimedia.org/wikipedia/commons/a/a3/Hepaticfailure.jpg>



Splenomegaly

<http://rtisus.com/resources/library/teaching-files/spleen/355875.jpg>

Complications of Cirrhosis (Quiz)



**Give reasons :
Ascites occurs in liver
cirrhosis**

Complications of Cirrhosis (Quiz)



Give reasons :
Ascites occurs in liver cirrhosis

Reason

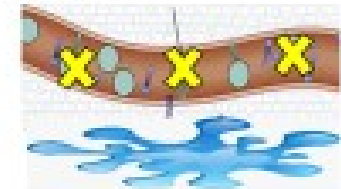
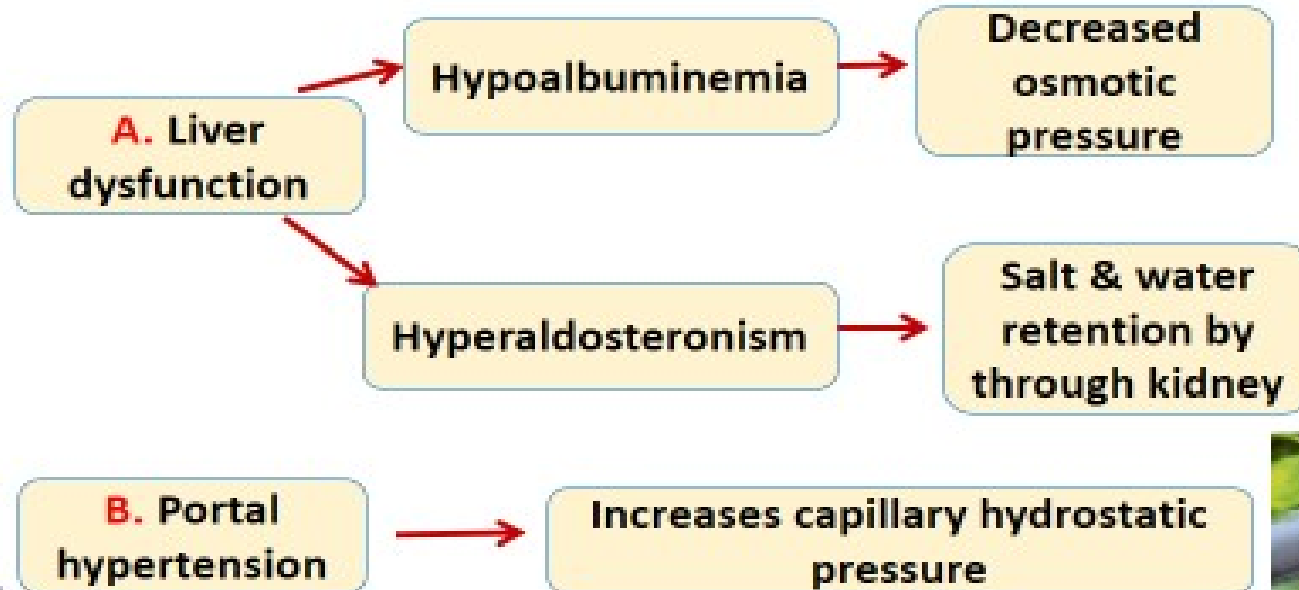
a. Ascites

Def: Collection of excess fluid in the peritoneal cavity.

Pathogenesis:



<https://upload.wikimedia.org/wikipedia/commons/1/12/Hepatichelone.jpg>



Effects of cirrhosis on blood tests (Quiz)



State whether these tests are high or low in liver cirrhosis

Transaminases (AST ,ALT)

Platelet count

WBC count

Bilirubin

Alkaline phosphatase

RBC count

Prothrombin time

Effects of cirrhosis on blood tests (Quiz)



State whether these tests are high or low in liver cirrhosis

Transaminases (AST ,ALT) H

Platelet count L

WBC count L

Bilirubin H

Alkaline phosphatase H

RBC count L

Prothrombin time H

Keypoints



- Cirrhosis is conversion of normal hepatic architecture into structurally abnormal nodules by fibrosis
-
- Pathogenesis of cirrhosis involves activation of Ito cells that are responsible for collagen deposition
- Effects & Complications of cirrhosis
- Pathogenesis of Portal Hypertension
- Pathogenesis of ascites

Prevention



- Do not drink alcohol if you have cirrhosis. If you have liver disease, you should avoid alcohol.
- Eat a healthy diet. Choose a plant-based diet that's full of fruits and vegetables. Select whole grains and lean sources of protein. Reduce the amount of fatty and fried foods you eat.

Prevention



- Maintain a healthy weight to avoid fatty liver.
- Avoid high risk behaviors like sharing needles and having unprotected sex.
- Hepatitis B vaccination.

Treatment of Liver Cirrhosis



- **Specific therapies according to cause:**
 - Prednisone and azathioprine - For autoimmune hepatitis
 - Antiviral agents - For hepatitis B and C

Treatment of Liver Cirrhosis



- **Specific therapies according to cause:**
 - Phlebotomy - For hemochromatosis
 - Ursodeoxycholic acid - For primary biliary cirrhosis
 - Trientine and zinc - For Wilson disease
 - Once cirrhosis develops, treatment is aimed at the management of complications as they arise.

Ascites



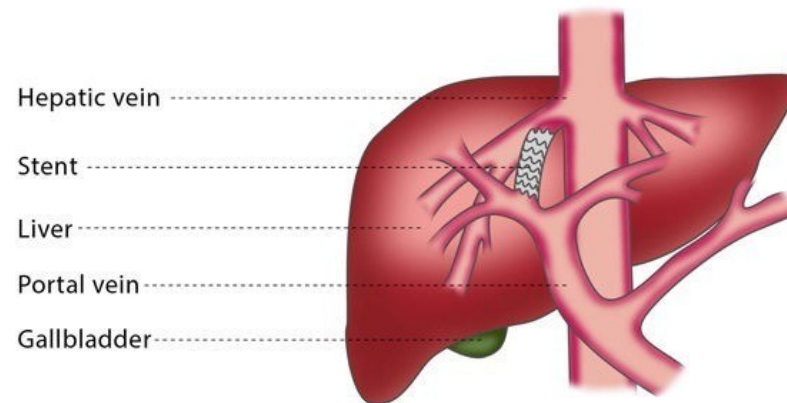
- Ascites
 - Sodium restriction
 - Diuretics
 - Large-volume paracentesis
 - Shunts

Variceal Bleeding



- Injection sclerotherapy of gastric varices
- Endoscopic band ligation of esophageal varices
- TIPS procedure if failed previous measures

Transjugular intrahepatic portosystemic shunt (TIPS)



Hepatic Encephalopathy



- Hepatic encephalopathy
 - Lactulose
 - Antibiotics

Liver Transplantation



- Patients should be referred for liver transplantation if hepatic decompensation starts.

References



- Andreoli and Carpenter's Cecil Essentials of Medicine (8th edition)
- Toronto Notes 2017

Suggested Textbooks



Neil D. Theise. Liver and gall bladder. In Robbins and Cotran
pathologic basis of disease, 10th edition. Kumar, Abbas &
Aster (eds). Elsevier Saunders. Pages 637-676

